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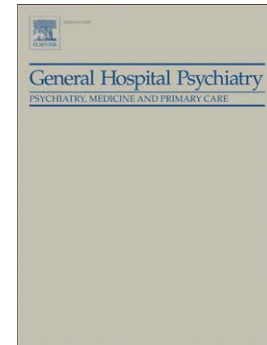
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Mild to moderate clozapine-induced gastrointestinal hypomotility should not require cessation of clozapine

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To the editors,

We read the review on clozapine-induced gastrointestinal hypomotility (CIGH) by West et al.¹ with interest and welcome the further highlighting of this adverse effect spectrum. However, the authors' use of the term CIGH is misleading and the recommendation to withdraw clozapine in people with CIGH may seriously disadvantage people experiencing treatment-resistant schizophrenia.

The authors define CIGH as "a paralytic ileus leading to a clinical condition similar to bowel obstruction". However, the term CIGH was coined in 2008² and refers to the effects of clozapine in slowing transit throughout the gastrointestinal tract.³⁻⁷ Clozapine impairs gut motility dramatically and this may result in an array of clinical presentations, from mild constipation and delayed gastric emptying at one end, to paralytic ileus, toxic megacolon and possibly death at the other. In other words, paralytic ileus and other life-threatening complications of CIGH, conditions that necessitate urgent medical and possibly surgical intervention, are but a small sub-set of the CIGH spectrum

Mild to moderate CIGH is very common, probably occurring in most people taking clozapine. Radiopaque marker studies show that 50-80% of clozapine-treated patients have significant gastrointestinal hypomotility,^{3,4} with one study finding a median colonic transit time of 104.5 hours for clozapine-treated patients, > 4 times normative values.⁴ A recent systematic review found constipation prevalence rates of least 30% in clozapine users.⁸ Severe complications of CIGH, such as ileus, are rare, with an estimated prevalence of around 0.4% of clozapine users,⁴ albeit with a high case-fatality rate.² The apparently precipitate nature of severe CIGH may also result in sudden death without the underlying cause having been identified even at autopsy.⁶

West et al recommend that "once CIGH has occurred clozapine should be halted". Whilst prompt withdrawal of clozapine is mandatory if paralytic ileus or other severe complications of CIGH develop, it is inappropriate for mild to moderate CIGH, which responds to assertive monitoring and prophylactic laxative use (e.g. the Porirua Protocol).⁵ Clozapine is a superior antipsychotic for treatment-resistant schizophrenia, significantly improving outcomes for many. An analysis of cause-specific mortality in 66,881 patients with schizophrenia found clozapine was associated with the lowest overall mortality risk (0.74; $p < 0.0001$) compared with no medication or other antipsychotic use.⁹ Discontinuing clozapine is often followed by significant relapse, deterioration in functioning, re-hospitalisation, and increased rates of compulsory treatment (e.g. Atkinson et al, 2007).¹⁰ Should West et al.'s recommendation of clozapine withdrawal in the presence of CIGH be taken literally then unnecessary relapse and net harm would follow for thousands of patients worldwide.

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